State by state...There's a way

ALABAMA
Sign on the right–
"Dispense as Written" line

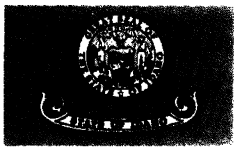
ALASKA
"Dispense as Written"

ARIZONA
Sign on the left–
"Dispense as Written" line

ARKANSAS
"Dispense as Written"

CALIFORNIA
"Do Not Substitute"

HAWAII
"Do Not Substitute"



IDAHO
Sign on the right–
"Dispense as Written" line

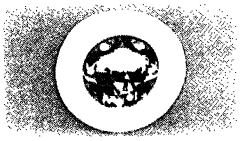
ILLINOIS
Check box–
"May Not Substitute"

INDIANA
Sign on the left–
"Dispense as Written" line

IOWA
"No Substitution"
or "D.A.W."

MASSACHUSETTS
"No Substitution"

MICHIGAN
"Dispense as Written"



MINNESOTA
"Dispense as Written"

MISSISSIPPI
"Dispense as Written"

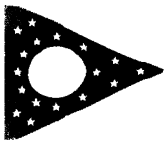
MISSOURI
Sign on the right–
"Dispense as Written" line

NEW MEXICO
"No Substitution"

NEW YORK
Write "D.A.W." in box

NORTH CAROLINA
Sign on the right–
"Dispense as Written" line

NORTH DAKOTA
Sign on the right–
"Dispense as Written" line



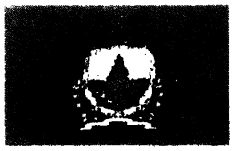
OHIO
"Dispense as Written"

SOUTH DAKOTA
Sign on the right–
"Dispense as Written" line

TENNESSEE
Sign bottom line–
"Dispense as Written"

TEXAS
Sign on the right–
"Dispense as Written" line

UTAH
"Dispense as Written"



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"No Substitution"

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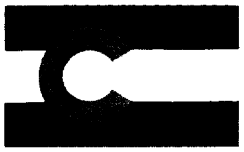
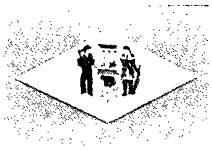
to "flag" your prescription...



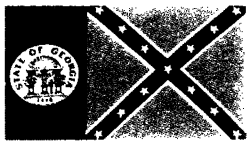
COLORADO
"Dispense as Written"

CONNECTICUT
"No Substitution"



DELAWARE
Sign top line—
"Dispense as Written"

FLORIDA
"Medically Necessary"



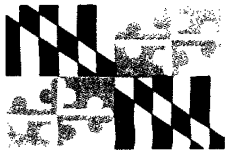
GEORGIA
"Brand Necessary"

KANSAS
"Dispense as Written"

KENTUCKY
"Do Not Substitute"

LOUISIANA
"No Substitution" or
"Dispense as Written"

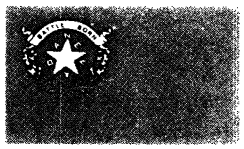
MAINE
Check box— ☐
"Do Not Substitute"



MARYLAND
"Do Not Substitute"

MONTANA
"Medically Necessary"

NEBRASKA
"No Drug Product Selection"
or "N.D.P.S."



NEVADA
Check box— ☐
"Dispense only as Written"

NEW HAMPSHIRE
"Medically Necessary"

NEW JERSEY
Initial on the right—
"Do Not Substitute" line

OKLAHOMA
"Do Not Substitute"

OREGON
"No Substitution"

PENNSYLVANIA
Sign on the left—
"Do Not Substitute" line

RHODE ISLAND
"Dispense as Written" line

SOUTH CAROLINA
Sign on the left—
"Dispense as Written" line

VIRGINIA
Sign on the right—
"Dispense as Written" line

WASHINGTON
Sign on the right—
"Dispense as Written" line

WEST VIRGINIA
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"Brand Necessary" line

WISCONSIN
"No Substitution"

WYOMING
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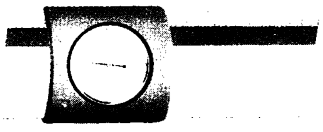
***CAPOTEN® (captopril tablets) may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. Overall, the most frequently occurring adverse reactions associated with CAPOTEN are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited. See INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS in the brief summary on the adjacent page.**

1. Croog SH, Levine S, Testa MA, et al: The effects of antihypertensive therapy on the quality of life. N Engl J Med 314(26):1657-1664, 1986.
2. Data on file, University of Connecticut.

THE



DIFFERENCE

THE QUALITY OF LIFE CAPOTEN® (captopril tablets) DIFFERENCE

CAPOTEN® TABLETS
Captopril Tablets

INDICATIONS: Hypertension – CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

CONTRAINDICATIONS: CAPOTEN is contraindicated in patients who are hypersensitive to this product.

WARNINGS: Neutropenia/Agranulocytosis – Neutropenia (≤ 1000/mm³) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine less than 1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during the subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors. **Evaluation of the hypertensive or heart failure patient should always include assessment of renal function.** If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever). If infection is suspected, perform white cell counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count < 1000/mm³) withdraw captopril and closely follow the patient's course.

Proteinuria: Total urinary proteins > 1 g per day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (> 150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy with captopril, patients with prior renal disease or those receiving captopril at doses > 150 mg per day, should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension: Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]). In heart failure, where the blood pressure was either normal or low, transient decreases in mean blood pressure > 20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function* – Hypertension – Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure – About 20% of patients develop stable elevations of BUN and serum creatinine > 20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis* – A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction. *Surgery/Anesthesia* – If hypotension occurs during surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension – Patients on Diuretic Therapy* – Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial of captopril dose in patients on diuretics, especially those recently placed on diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

Agents Having Vasodilator Activity – In heart failure patients, vasodilators should be administered with caution.

Agents Causing Renin Release – Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity – The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium – Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis – Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C: There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. CAPOTEN (captopril) should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal – About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic – Neutropenia/agranulocytosis has occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic – Rash, (usually maculopapular, rarely urticarial), often with pruritus, and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity, have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients – reversible on discontinuance of captopril therapy. One case of laryngeal edema has been reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular – Hypotension may occur; see WARNINGS and PRECAUTIONS [Drug Interactions] for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia – Approximately 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice, and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertension patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg and 50 mg also available in bottles of 1000), and in UNIMATIC® unit-dose packs of 100 tablets. (J3-658J)

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528-506 Issued: January 1988

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Sucralfate:	
All patients	79.4%
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Cimetidine:	
All patients	76.3%
Smokers	62.5%

*Significantly greater than cimetidine smoker group ($P<.05$).

Carafate has a unique, nonsystemic mode of action that enhances the body's own ulcer healing ability and protects the damaged mucosa from further injury.

When your ulcer patient is a smoker, prescribe the ulcer medication that won't go up in smoke: safe, nonsystemic Carafate.

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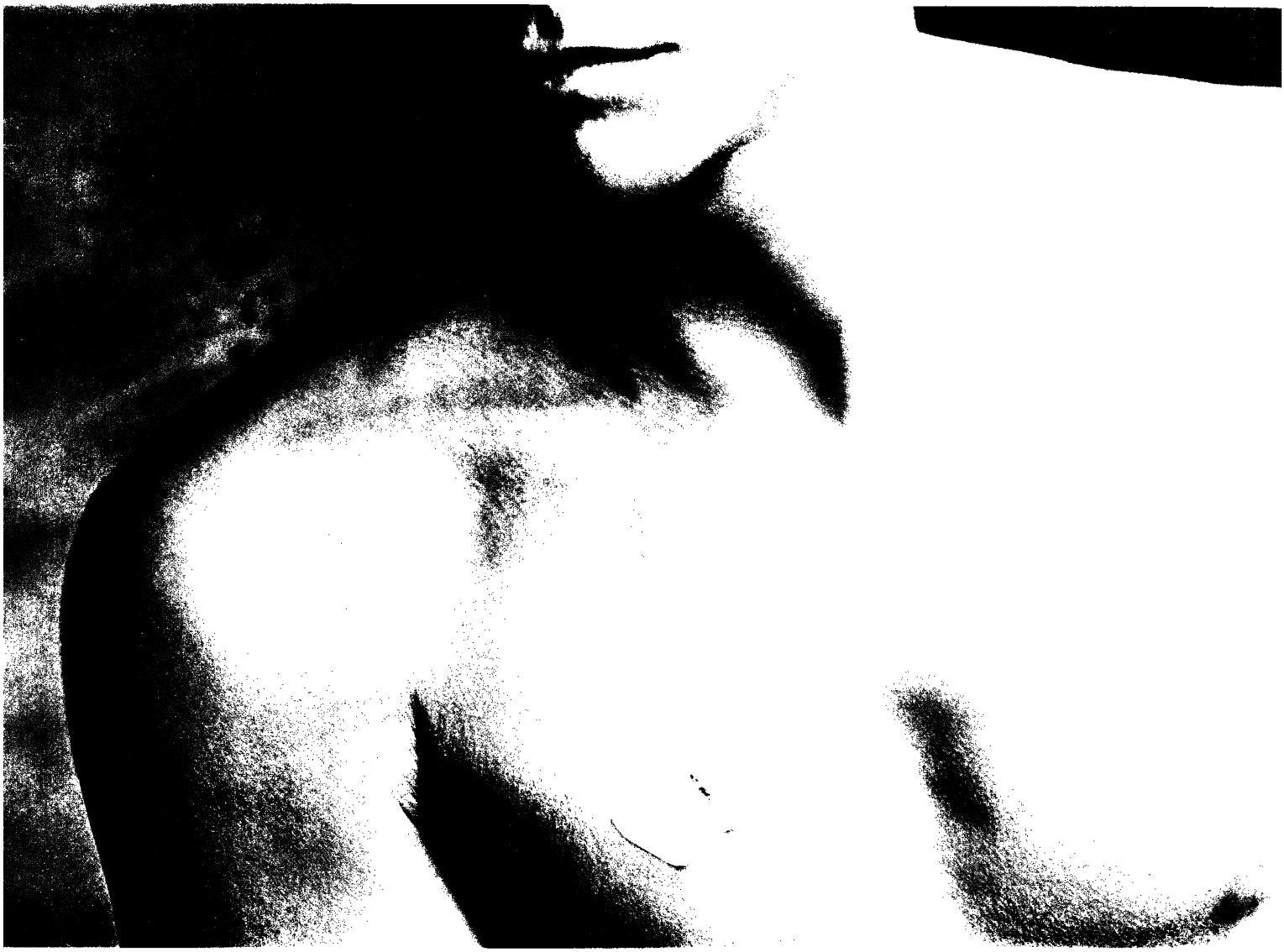
Please see adjoining page for references and brief summary of prescribing information.

1594H7



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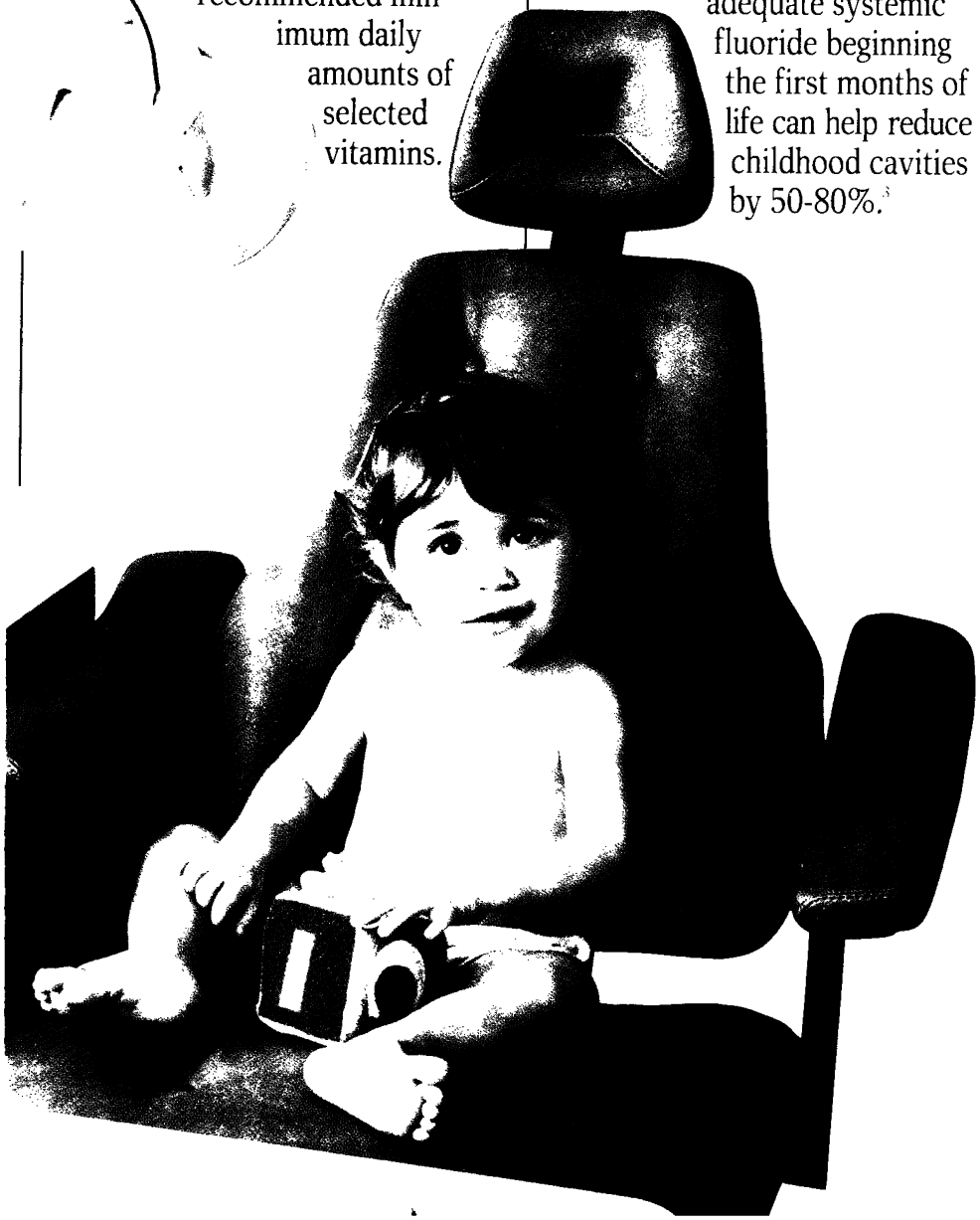

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References:

1. Moss SJ: The worldwide decline in caries prevention. in Mead Johnson Clinical Report Series. Clinical Importance of Fluoride Nutrition in Infants. Children. and Young Adults. Chicago. Pragmaton: 1985. Number 1. p. 2.

2. Newbrun E: How fluoride works: Topical vs. systemic action. in Mead Johnson Clinical Report Series. Clinical Importance of Fluoride Nutrition in Infants. Children. and Young Adults. Chicago. Pragmaton: 1985. Number 1. p. 5.

3. Aasenden R and Peebles T: Effects of fluoride supplementation from birth on human deciduous and permanent teeth. *Arch Oral Biol* 1974;19:321.

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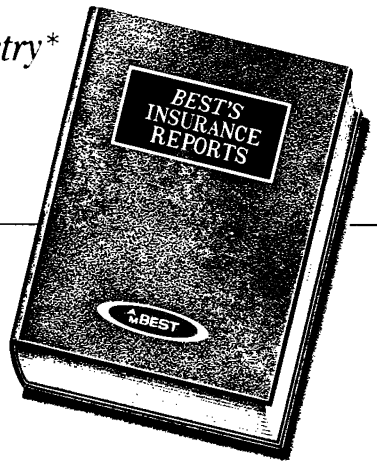

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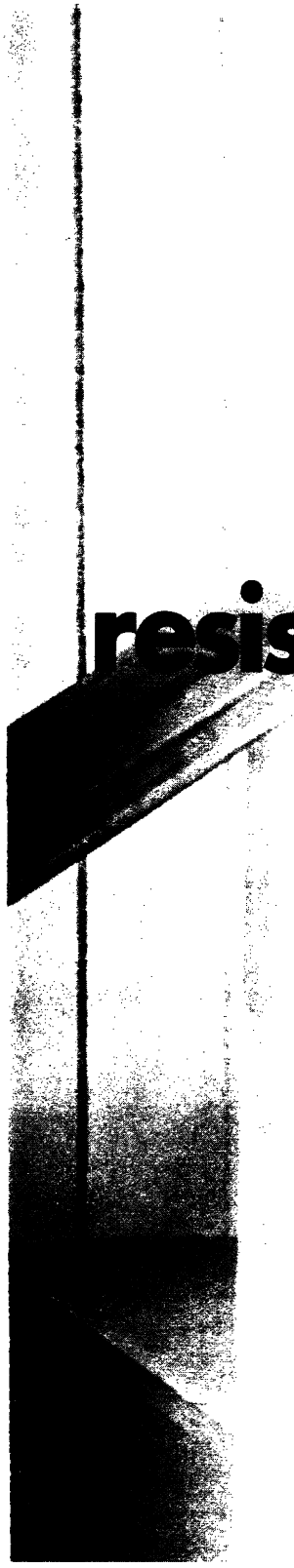

IN HYPERTENSION

resistance in the elderly[1]

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- ☐ Low incidence of fatigue,[2,3] impotence[2,3] and cold extremities[2-4]

Contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, and severe bradycardia.

See next page for references and Brief Summary of Product Information, which includes a listing of reported adverse reactions.

TRANDATE® *b.i.d.*

labetalol HCl/Glaxo *100 mg/200 mg tablets*

Because it also vasodilates

References: 1. Holtzman JL, Finley D, Johnson B, et al: The effects of single-dose atenolol, labetalol, and propranolol on cardiac and vascular function. *Clin Pharmacol Ther* 1986;40:268-273. 2. Due DL, Giguere GC, Plachetka JR: Postmarketing comparison of labetalol and propranolol in hypertensive patients. *Clin Ther* 1986;8(6):624-631. 3. Burris JF, Goldstein J, Zager PG, et al: Comparative tolerability of labetalol versus propranolol, atenolol, pindolol, metoprolol, and nadolol. *J Clin Hypertens* 1986;3:1-9. 4. Erb RJ, Plachetka JR: Thermographic evaluation of the peripheral vascular effects of labetalol and propranolol. *Curr Ther Res* 1985;28(1):68-73.

TRANDATE® Tablets
(labetalol hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in TRANDATE® Tablets product labeling.

INDICATIONS AND USAGE: TRANDATE® Tablets are indicated in the management of hypertension. TRANDATE Tablets may be used alone or in combination with other antihypertensive agents, especially thiazide and loop diuretics.

CONTRAINDICATIONS: TRANDATE® Tablets are contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, and severe bradycardia (see **WARNINGS**).

WARNINGS: Cardiac Failure: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure. Beta-blockade carries a potential hazard of further depressing myocardial contractility and precipitating more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary labetalol HCl can be used with caution in patients with a history of heart failure who are well compensated. Congestive heart failure has been observed in patients receiving labetalol HCl. Labetalol HCl does not abolish the inotropic action of digitalis on heart muscle.

In Patients Without a History of Cardiac Failure: In patients with latent cardiac insufficiency, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or be given a diuretic, and the response should be observed closely. If cardiac failure continues despite adequate digitalization and diuretic, TRANDATE® therapy should be withdrawn (gradually, if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal: Angina pectoris has not been reported upon labetalol HCl discontinuation. However, hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after *abrupt* discontinuation of such therapy. When discontinuing chronically administered TRANDATE, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of one to two weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, TRANDATE administration should be reinstituted promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue TRANDATE therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (eg, Chronic Bronchitis and Emphysema): Patients with bronchospastic disease should, in general, not receive beta-blockers. TRANDATE may be used with caution, however, in patients who do not respond to, or cannot tolerate, other antihypertensive agents. It is prudent, if TRANDATE is used, to use the smallest effective dose, so that inhibition of endogenous or exogenous beta-agonists is minimized.

Pheochromocytoma: Labetalol HCl has been shown to be effective in lowering blood pressure and relieving symptoms in patients with pheochromocytoma. However, paradoxical hypertensive responses have been reported in a few patients with this tumor; therefore, use caution when administering labetalol HCl to patients with pheochromocytoma.

Diabetes Mellitus and Hypoglycemia: Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (eg, tachycardia) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces the release of insulin in response to hyperglycemia; it may therefore be necessary to adjust the dose of antidiabetic drugs.

Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy prior to major surgery is controversial. Protracted severe hypotension and difficulty in restarting or maintaining a heartbeat have been reported with beta-blockers. The effect of labetalol HCl's alpha-adrenergic activity has not been evaluated in this setting.

A synergism between labetalol HCl and halothane anesthesia has been shown (see **Drug Interactions** under **PRECAUTIONS**).

PRECAUTIONS: General: ***Impaired Hepatic Function:*** TRANDATE® Tablets should be used with caution in patients with impaired hepatic function since metabolism of the drug may be diminished.

Jaundice or Hepatic Dysfunction: On rare occasions, labetalol HCl has been associated with jaundice (both hepatic and cholestatic). It is therefore recommended that treatment with labetalol HCl be stopped immediately should a patient develop jaundice or laboratory evidence of liver injury. Both have been shown to be reversible on stopping therapy.

Information for Patients: As with all drugs with beta-blocking activity, certain advice to patients being treated with labetalol HCl is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects. While no incidence of the abrupt withdrawal phenomenon (exacerbation of angina pectoris) has been reported with labetalol HCl, dosing with TRANDATE Tablets should not be interrupted or discontinued without a physician's advice. Patients being treated with TRANDATE Tablets should consult a physician at any sign of impending cardiac failure. Also, transient scalp tingling may occur, usually when treatment with TRANDATE Tablets is initiated (see **ADVERSE REACTIONS**).

Laboratory Tests: As with any new drug given over prolonged periods, laboratory parameters should be observed over regular intervals. In patients with concomitant illnesses, such as impaired renal function, appropriate tests should be done to monitor these conditions.

Drug Interactions: In one survey, 2.3% of patients taking labetalol HCl in combination with tricyclic antidepressants experienced tremor as compared to 0.7% reported to occur with labetalol HCl alone. The contribution of each of the treatments to this adverse reaction is unknown, but the possibility of a drug interaction cannot be excluded.

Drugs possessing beta-blocking properties can blunt the bronchodilator effect of beta-receptor agonist drugs in patients with bronchospasm; therefore, doses greater than the normal antiasthmatic dose of beta-agonist bronchodilator drugs may be required.

Cimetidine has been shown to increase the bioavailability of labetalol HCl. Since this could be explained either by enhanced absorption or by an alteration of hepatic metabolism of labetalol HCl, special care should be used in establishing the dose required for blood pressure control in such patients.

Synergism has been shown between halothane anesthesia and intravenously administered labetalol HCl. During controlled hypotensive anesthesia using labetalol HCl in association with halothane, high concentrations (3% or above) of halothane should not be used because the degree of hypotension will be increased and because of the possibility of a large reduction in cardiac output and an increase in central venous pressure. The anesthesiologist should be informed when a patient is receiving labetalol HCl.

Labetalol HCl blunts the reflex tachycardia produced by nitroglycerin without preventing its hypotensive effect. If labetalol HCl is used with nitroglycerin in patients with angina pectoris, additional antihypertensive effects may occur.

Drug/Laboratory Test Interactions: The presence of a metabolite of labetalol in the urine may result in falsely increased levels of urinary catecholamines when measured by a nonspecific trihydroxyindole (THI) reaction. In screening patients suspected of having a pheochromocytoma and being treated with labetalol HCl, specific radioenzymatic or high performance liquid chromatography assay techniques should be used to determine levels of catecholamines or their metabolites.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term oral dosing studies with labetalol HCl for 18 months in mice and for two years in rats showed no evidence of carcinogenesis. Studies with labetalol HCl using dominant lethal assays in rats and mice and exposing microorganisms according to modified Ames tests showed no evidence of mutagenesis.

Pregnancy: ***Teratogenic Effects: Pregnancy Category C:*** Teratogenic studies have been performed with labetalol in rats and rabbits at oral doses up to approximately six and four times the maximum recommended human dose (MRHD), respectively. No reproducible evidence of fetal malformations was observed. Increased fetal resorptions were seen in both species at doses approximating the MRHD. There are no adequate and well-controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects: Infants of mothers who were treated with labetalol HCl during pregnancy did not appear to be adversely affected by the drug. Oral administration of labetalol to rats during late gestation through weaning at doses of two to four times the MRHD caused a decrease in neonatal survival.

Labor and Delivery: Labetalol HCl given to pregnant women with hypertension did not appear to affect the usual course of labor and delivery.

Nursing Mothers: Small amounts of labetalol (approximately 0.004% of the maternal dose) are excreted in human milk. Caution should be exercised when TRANDATE Tablets are administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Most adverse effects are mild, transient, and occur early in the course of treatment. In controlled clinical trials of three to four months' duration, discontinuation of TRANDATE® Tablets due to one or more adverse effects was required in 7% of all patients. In these same trials, beta-blocker control agents led to discontinuation in 8% to 10% of patients, and a centrally acting alpha-agonist in 30% of patients.

The following adverse reactions were derived from multi-center, controlled clinical trials over treatment periods of three and four months. The rates, which ranged from less than 1% to 5% except as otherwise noted, are based on adverse reactions considered probably drug-related by the investigator. If all reports are considered, the rates are somewhat higher (eg, dizziness, 20%; nausea, 14%; fatigue, 11%).

Body as a Whole: Fatigue, asthenia, and headache.

Gastrointestinal: Nausea (6%), vomiting, dyspepsia, diarrhea, and taste distortion.

Central and Peripheral Nervous Systems: Dizziness (11%), paresthesia, and drowsiness.

Autonomic Nervous System: Nasal stuffiness, ejaculation failure, impotence, and increased sweating.

Cardiovascular: Edema and postural hypotension.

Respiratory: Dyspnea.

Skin: Rash.

Special Senses: Vision abnormality and vertigo.

The adverse effects were reported spontaneously and are representative of the incidence of adverse effects that may be observed in a properly selected hypertensive patient population, ie, a group excluding patients with bronchospastic disease, overt congestive heart failure, or other contraindications to beta-blocker therapy.

Clinical trials also included studies utilizing daily doses up to 2,400 mg in more severely hypertensive patients. The US therapeutic trials data base for adverse reactions that are clearly or possibly dose-related shows that the following side effects increased with increasing dose: dizziness, fatigue, nausea, vomiting, dyspepsia, paresthesia, nasal stuffiness, ejaculation failure, impotence, and edema.

In addition, a number of other less common adverse events have been reported in clinical trials or the literature:

Cardiovascular: Postural hypotension, including rarely, syncope.

Central and Peripheral Nervous Systems: Paresthesias, most frequently described as scalp tingling. In most cases, it was mild, transient, and usually occurred at the beginning of treatment.

Collagen Disorders: Systemic lupus erythematosus; positive antinuclear factor (ANF).

Eyes: Dry eyes.

Immunological System: Antimitochondrial antibodies.

Liver and Biliary System: Cholestasis with or without jaundice.

Musculoskeletal System: Muscle cramps; toxic myopathy.

Respiratory System: Bronchospasm.

Skin and Appendages: Rashes of various types, such as generalized maculopapular, lichenoid, urticarial, bullous lichen planus, psoriaform, and facial erythema; Peyronie's disease; reversible alopecia.

Urinary System: Difficulty in micturition, including acute urinary bladder retention.

Following approval for marketing in the United Kingdom, a monitored release survey involving approximately 6,800 patients was conducted for further safety and efficacy evaluation of this product. Results of this survey indicate that the type, severity, and incidence of adverse effects were comparable to those cited above.

Potential Adverse Effects: In addition, other adverse effects not listed above have been reported with other beta-adrenergic blocking agents.

Central Nervous System: Reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance or neuropsychometrics.

Cardiovascular: Intensification of AV block (see **CONTRAINDICATIONS**).

Allergic: Fever combined with aching and sore throat; laryngospasm; respiratory distress.

Hematologic: Agranulocytosis; thrombocytopenic or nonthrombocytopenic purpura.

Gastrointestinal: Mesenteric artery thrombosis; ischemic colitis.

The oculomucocutaneous syndrome associated with the beta-blocker practolol has not been reported with labetalol HCl.

Clinical Laboratory Tests: There have been reversible increases of serum transaminases in 4% of patients treated with labetalol HCl and tested, and more rarely, reversible increases in blood urea.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: DOSAGE MUST BE INDIVIDUALIZED. The recommended *initial* dosage is 100 mg *twice* daily whether used alone or added to a diuretic regimen. After two or three days, using standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg bid every two or three days. The usual *maintenance* dosage of labetalol HCl is between 200 and 400 mg *twice* daily. Before use, see complete prescribing information for dosage details.

HOW SUPPLIED: TRANDATE® Tablets, 100 mg, light orange, round, scored, film-coated tablets engraved on one side with "TRANDATE 100 GLAXO," bottles of 100 (NDC 0173-0346-43) and 500 (NDC 0173-0346-44) and unit dose packs of 100 tablets (NDC 0173-0346-47).

TRANDATE Tablets, 200 mg, white, round, scored, film-coated tablets engraved on one side with "TRANDATE 200 GLAXO," bottles of 100 (NDC 0173-0347-43) and 500 (NDC 0173-0347-44) and unit dose packs of 100 tablets (NDC 0173-0347-47).

TRANDATE Tablets, 300 mg, peach, round, scored, film-coated tablets engraved on one side with "TRANDATE 300 GLAXO," bottles of 100 (NDC 0173-0348-43) and 500 (NDC 0173-0348-44) and unit dose packs of 100 tablets (NDC 0173-0348-47).

TRANDATE Tablets should be stored between 2° and 30°C (36° and 86°F). TRANDATE Tablets in the unit dose boxes should be protected from excessive moisture.

September 1986

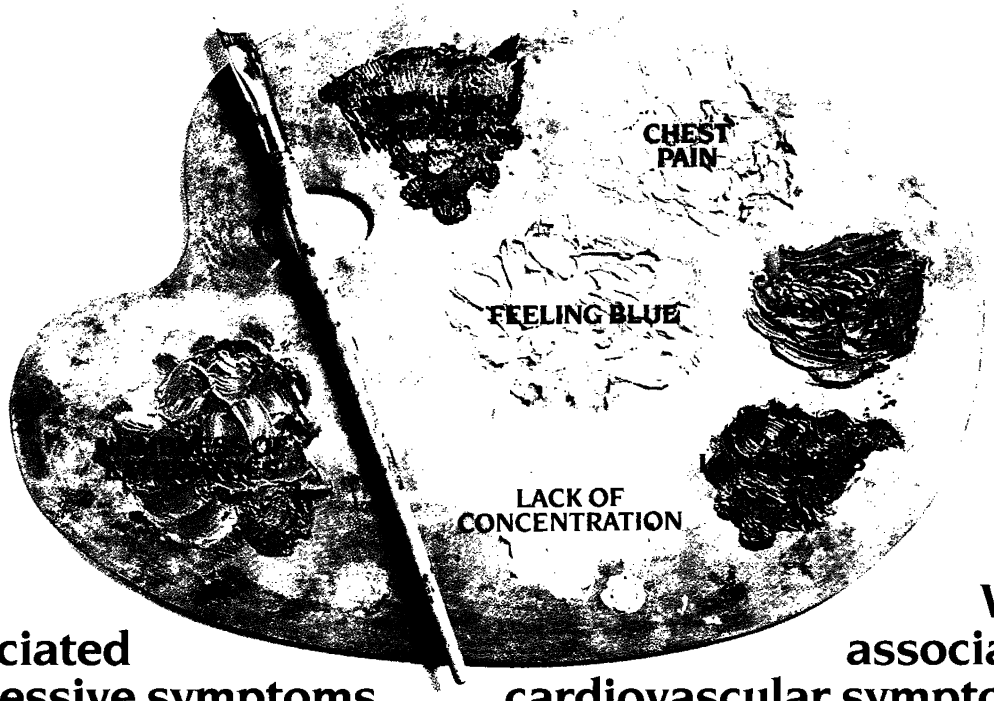
Glaxo Inc.
Research Triangle Park, NC 27709

The portrait of anxiety

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001 USA

Please see adjacent page for brief summary of prescribing information.

is often complicated



With associated depressive symptoms.

In double-blind, four-week clinical trials in 632 patients with moderate to severe anxiety therapy with XANAX was compared with placebo.

XANAX was significantly more effective ($P<.001$) than placebo in relieving the anxiety with over half of the patients showing marked to moderate improvement by the first evaluation period (one week).

In addition over 70% of these patients experienced associated moderate to severe depressed mood. XANAX was shown to be significantly more effective ($P<.014$) than placebo in improving the associated depressed mood.

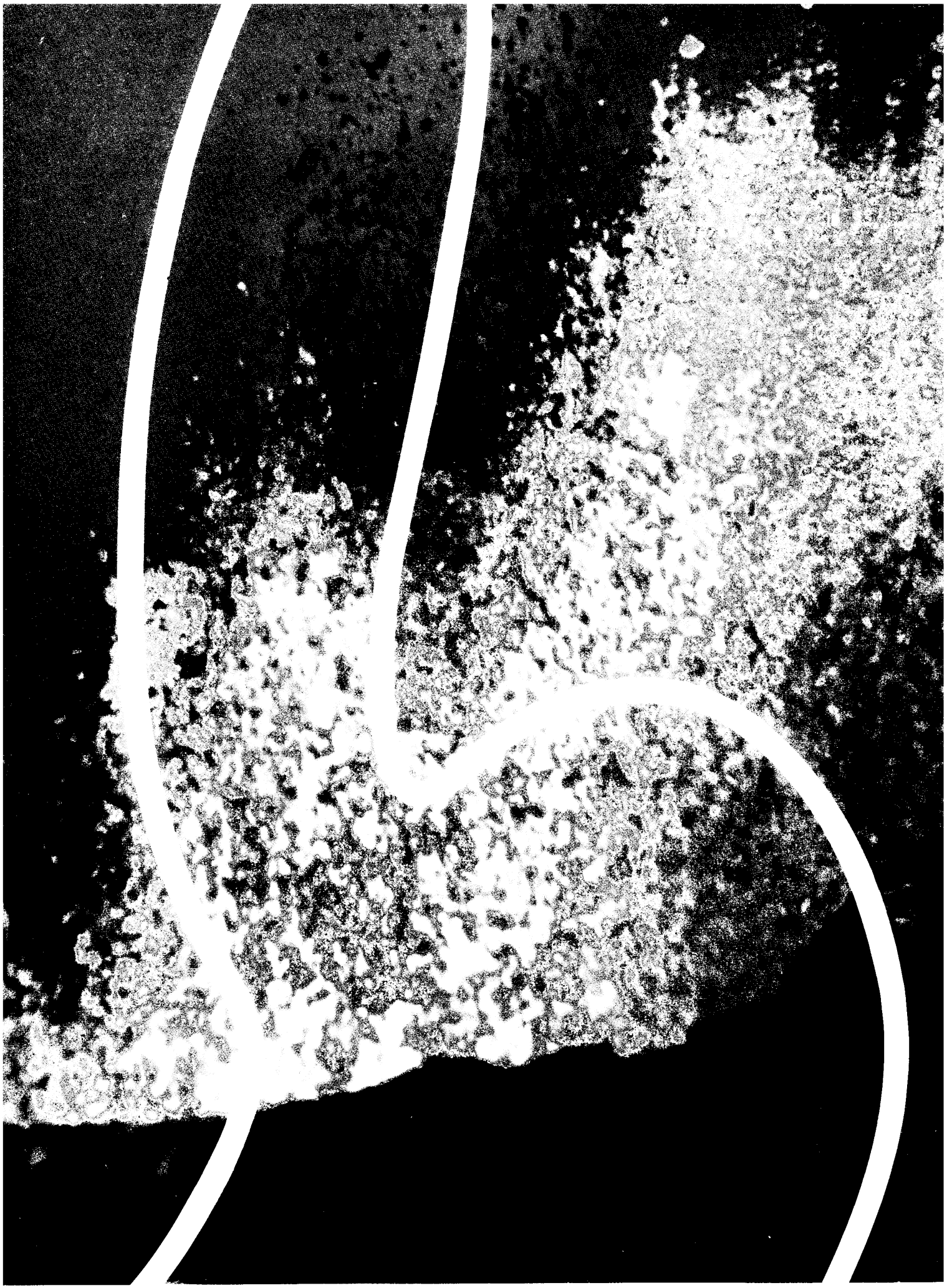
With associated cardiovascular symptoms.

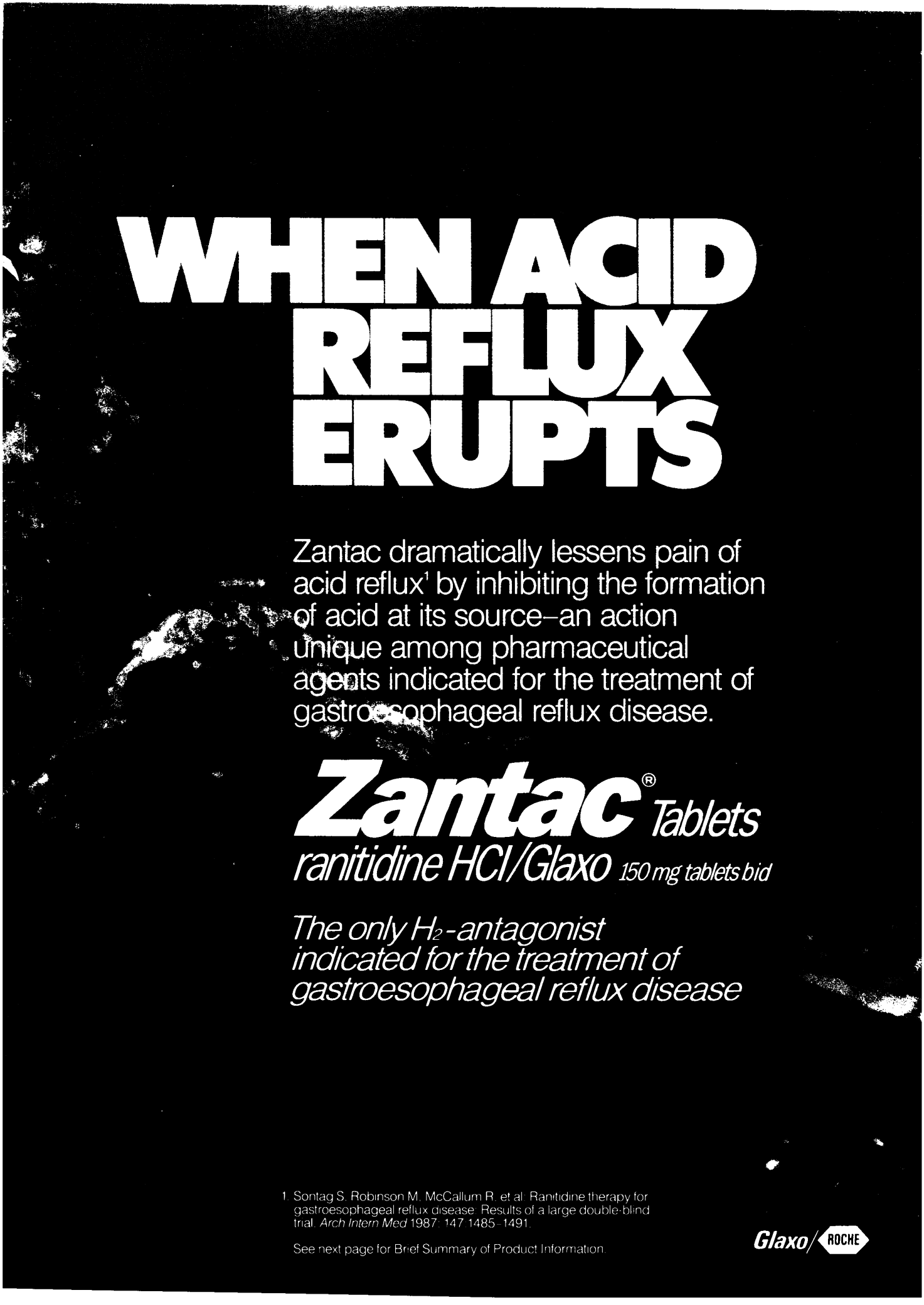
Almost 60% of patients in the study had anxiety with associated cardiovascular symptoms even though cardiovascular disease had been ruled out. XANAX was shown to effectively relieve anxiety including the associated cardiovascular symptoms.

XANAX the first of a unique class—the triazolobenzodiazepines.

- *Well tolerated*—Side effects if they occur are generally observed at the beginning of therapy and usually disappear with continued medication. Drowsiness and light-headedness were the most commonly reported adverse reactions.
- *Sustained efficacy*—No reported increase in dosage during 16-week clinical study once an appropriate dosage was achieved. Since long-term effectiveness of XANAX has not been established it is recommended that it not be used for longer than 16 weeks.
- *Simple dosage*—0.25 to 0.5 mg t.i.d.

for the relief of complicated anxiety




WHEN ACID REFLUX ERUPTS
Zantac dramatically lessens pain of acid reflux[1] by inhibiting the formation of acid at its source–an action unique among pharmaceutical agents indicated for the treatment of gastroesophageal reflux disease.
Zantac® Tablets
ranitidine HCl/Glaxo 150 mg tablets bid
The only H2-antagonist indicated for the treatment of gastroesophageal reflux disease
1. Sontag S, Robinson M, McCallum R, et al: Ranitidine therapy for gastroesophageal reflux disease. Results of a large double-blind trial. Arch Intern Med 1987; 147:1485-1491.
See next page for Brief Summary of Product Information.
Glaxo/ ROCHE

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BASF Group

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Spare your patients the extra cost—in calories, sodium and dollars.

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DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Effective antihypertensive* therapy...without the bananas

DAW
'DYAZIDE' AS WRITTEN.

* Not for initial therapy. See brief summary.

Before prescribing, see complete prescribing information in SK&F CO. literature or PDR. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: *Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.*

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. *If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake.* ***Associated widened QRS complex or arrhythmia requires prompt additional therapy.*** *Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.*

Precautions: *The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin[ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.*

Adverse Reactions: *Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.*

Supplied: ***'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.***

BRS-DZ;L45

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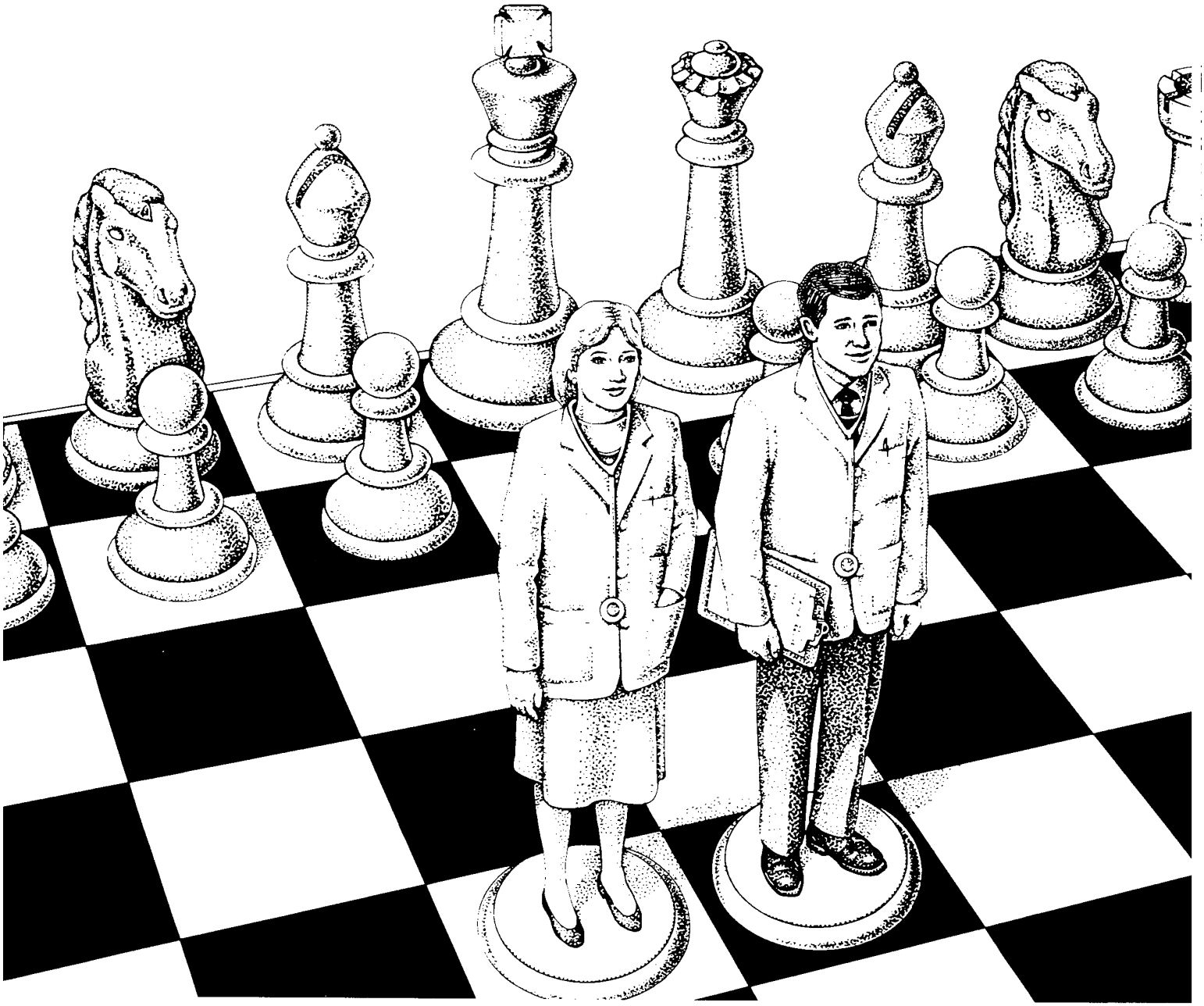

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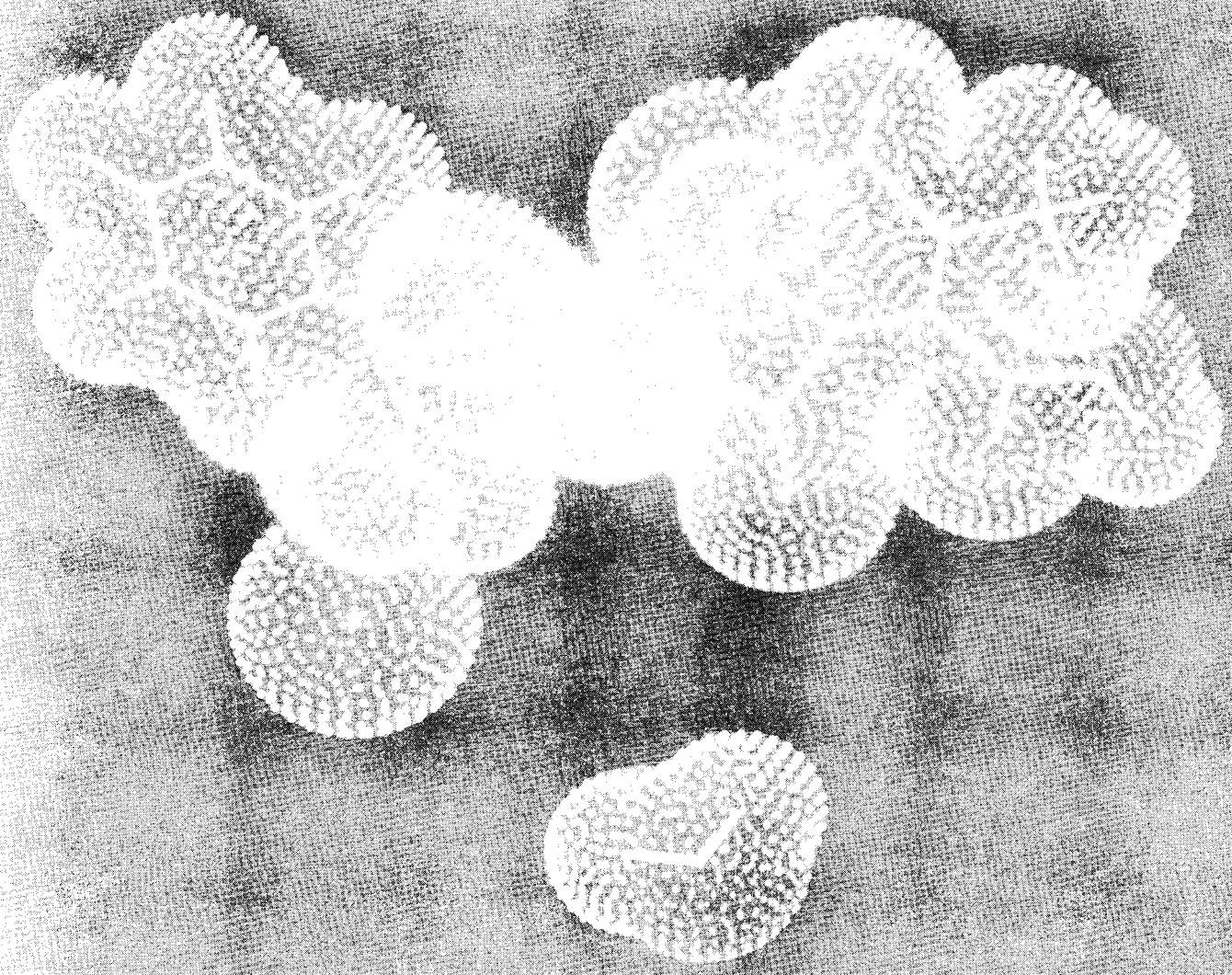
Cephalexin hydrochloride monohydrate



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Computer-generated molecular structure of cephalexin hydrochloride monohydrate

Convenient 500-mg b.i.d. dosage and demonstrated effectiveness for treatment of:

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- ☐ pharyngitis‡

- New hydrochloride salt form of cephalexin—requires no conversion in the stomach before absorption
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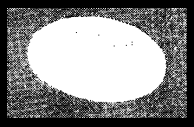

- May be taken without regard to meals

For other indicated infections, 250-mg tablets available for q.i.d. dosage

Priced less than Keflex (cephalexin)

Keftab is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-sensitive patients.

Penicillin is the drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever.

*Due to susceptible strains of
†Due to susceptible strains of
‡Due to susceptible strains of

KEFTAB™
(cephalexin hydrochloride monohydrate)

Summary: Consult the package literature for prescribing information.

Indications and Usage:

Respiratory tract infections caused by susceptible strains of *Streptococcus pneumoniae* and group A β-hemolytic streptococci.

Skin and skin structure infections caused by susceptible strains of *Staphylococcus aureus* and/or β-hemolytic streptococci.

Bone infections caused by susceptible strains of *S aureus* and/or *Proteus mirabilis.*

Genitourinary tract infections, including acute prostatitis, caused by susceptible strains of *Escherichia coli, P mirabilis,* and *Klebsiella* sp.

Contraindication: Known allergy to cephalosporins.

Warnings: KEFTAB SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:

- Discontinue Keftab in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Keftab should be administered cautiously in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy and lactation. Cephalexin is excreted in mother's milk. Exercise caution in prescribing Keftab for these patients.
- Safety and effectiveness in children have not been established.

Adverse Reactions:

- *Gastrointestinal,* including diarrhea and, rarely, nausea and vomiting. Transient hepatitis and cholestatic jaundice have been reported rarely.
- *Hypersensitivity* in the form of rash, urticaria, angioedema, and, rarely, erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis.
- *Anaphylaxis* has been reported.
- *Other reactions* have included genital/anal pruritus, genital moniliasis, vaginitis/vaginal discharge, dizziness, fatigue, headache, eosinophilia, neutropenia, and thrombocytopenia; reversible interstitial nephritis has been reported rarely.
- Cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment.
- *Abnormalities in laboratory test results* included slight elevations in aspartate aminotransferase (AST, SGOT) and alanine aminotransferase (ALT, SGPT). False-positive reactions for glucose in the urine may occur with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (Glucose Enzymatic Test Strip, USP, Lilly).

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DON'T OVERLOOK THE

WHEN TREATING

More than 8 out of 10 patients who present with allergic rhinitis may suffer from concurrent allergic ocular signs and symptoms —itchy, scratchy eyes, erythema and edema, tearing, irritation—according to two recent studies.[1,2]

What's worse is that many patients don't mention their ocular symptoms when reporting allergic rhinitis unless specifically asked.

So look for the overlapping clinical symptoms and then confidently treat allergic ocular disorders* with OPTICROM. It has a proven clinical record of efficacy with freedom from serious side effects or ocular toxicity.

OPTICROM 4%

THE SOLUTION FOR ALLERGIC OCULAR DISORDERS

Reference: 1,2. Data on file, Fisons Corporation
Independent Studies by DTW Market Research Group July 1985

*See below for listing of certain allergic ocular disorders

INDICATIONS AND USAGE: OPTICROM is indicated in the treatment of certain allergic ocular disorders referred to by the terms vernal keratoconjunctivitis, vernal conjunctivitis, giant papillary conjunctivitis, vernal keratitis, and allergic keratoconjunctivitis. The etiologic factors are unknown, but common airborne allergens and contact lenses have been implicated.[1]

Symptomatic response to therapy (decreased itching, tearing, redness, and discharge) is usually evident within a few days, but longer treatment for up to six weeks is sometimes required. Once symptomatic improvement has been established, therapy should be continued for as long as needed to sustain improvement.

If required, corticosteroids may be used concomitantly with OPTICROM.

Users of soft (hydrophilic) contact lenses should refrain from wearing lenses while under treatment with OPTICROM (see **Contraindications**). Wear can be resumed within a few hours after discontinuation of the drug.

CONTRAINDICATIONS: OPTICROM is contraindicated in those patients who have shown hypersensitivity to cromolyn sodium or to any of the other ingredients.

As with all ophthalmic preparations containing benzalkonium chloride, patients are advised not to wear soft contact lenses during treatment with OPTICROM.

PRECAUTIONS: General: Patients may experience a transient stinging or burning sensation following application of OPTICROM.

The recommended frequency of administration should not be exceeded. The dose for adults and children is 1-2 drops in each eye 4-6 times a day at regular intervals.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long term studies in mice (12 months intraperitoneal treatment followed by six months observation), hamsters (12 months intraperitoneal treatment followed by 12 months observation), and rats (18 months subcutaneous treatment) showed no neoplastic effect of cromolyn sodium.

No evidence of chromosomal damage or cytotoxicity was obtained in various mutagenesis studies.

No evidence of impaired fertility was shown in laboratory animal reproduction studies.

Pregnancy: Pregnancy Category B. Reproduction studies with cromolyn sodium administered parenterally to pregnant mice, rats and rabbits in doses up to 338 times the human clinical doses produced no evidence of fetal malformations. Adverse fetal effects (increased resorption and decreased fetal weight) were noted only at the very high parenteral doses that produced maternal toxicity. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when OPTICROM is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below the age of 4 years have not been established.

ADVERSE REACTIONS: The most frequently reported adverse reaction attributed to the use of OPTICROM, on the basis of reoccurrence following readministration, is transient ocular stinging or burning upon instillation.

The following adverse reactions have been reported as infrequent events. It is unclear whether they are attributable to the drug: conjunctival injection, watery eyes, itchy eyes, dryness around the eye, puffy eyes, eye irritation, styes.

CAUTION: Federal law prohibits dispensing without prescription.

REFERENCE: 1. Allansmith MR, Abelson MB. Ocular Allergies. In: *The Cornea*, ed. by G. Smolin, RA Thoft, Little, Brown and Co., Boston/Toronto, 1983: 231-43.

See package insert for full prescribing information.

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WE HAVE FULL- AND PART-TIME LOCUM TENENS opportunities available with guaranteed incomes and paid malpractice. For more information, contact John Smith, Locum Tenens, Inc (A Division of Jackson and Coker), 400 Perimeter Center Terrace, Ste 760 WJM, Atlanta, GA 30346; Tel. 1 (800) 544-1987.

ARIZONA-BASED PHYSICIAN recruiting firm has opportunities coast-to-coast. "Quality Physicians for Quality Clients since 1972." Call (602) 990-8080; or send CV to Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252.

SAN FRANCISCO—ONE HOUR. Multispecialty group in a growing community is now accepting applications for positions available in Family Practice and Internal Medicine. First year includes guaranteed salary plus incentive. Excellent benefits including malpractice, life, health, and disability insurance. Send CV to Number 51, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

WASHINGTON, OREGON. Practice opportunities in urgent care and emergency department settings throughout the northwest. Malpractice provided in most locations. Competitive salaries. Recreational activities abound. Write or call L. Poschman, Northwest Emergency Physicians, 11808 Northup Way, Ste 110, Bellevue, WA 98005; (206) 828-6799.

SOUTH CENTRAL WYOMING. Immediate practice opportunity for BC/BE Urologist. Well-equipped JCAH hospital for a service area of approximately 20,000 population. No state or city income tax. Relocation incentives. Superior hunting, fishing, camping, snowmobiling. Three hours to Colorado ski area, five hours to Jackson Hole. One and one-half hours to the mountains. If interested, please send CV and references to D. Abels, DO, Chairman, Recruiting Committee or Richard Mills, Executive Director, Memorial Hospital of Carbon County, Rawlins, WY 82301; (307) 324-2221.

PHYSICIANS WANTED

NEUROLOGIST. Visalia Medical Clinic, Inc, a 37 physician multispecialty group, is searching for a Neurologist to enter an active practice. Located in the San Joaquin Valley in California and serving a market area of approximately 350,000. Excellent hospital services and facilities. BC/BE. Compensation is incentive oriented with rapid advancement to full partnership. Excellent fringe benefits. Please respond to John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

DERMATOLOGIST. Visalia Medical Clinic has an opening for a BC/BE Dermatologist now staffed by one physician who has been with the Clinic for 15 years. Located in the San Joaquin Valley in central California and population approximately 350,000. Progressive city of 62,000, near national parks and the ocean. Compensation is incentive oriented with advancement to full partnership after one year. Excellent fringe benefits. If interested, CV to John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

NEUROSURGERY. Visalia Medical Clinic has an opening for a BC/BE Neurological Surgeon to enter an immediate and active practice. Located in the San Joaquin Valley of California, serving a market area of approximately 350,000 citizens. Two Neurosurgeons presently serving this area. Excellent hospital services and facilities. Must be BC/BE. Compensation is incentive oriented with advancement to full partnership after one year. Excellent fringe benefits. John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

CALIFORNIA. Emergency Medicine Faculty Positions. Immediate opportunities available for career-oriented Emergency Physicians who possess excellent clinical and teaching skills to join the faculty of Emergency Medicine department. BC in Family Practice, Internal Medicine, Surgery, and/or BE in Emergency Medicine. Our facility, located in southern California, averages 38,000 Emergency department visits per year, is a level II trauma center, regional burn center and neonatology intensive care center. These positions require a teaching commitment in a university-affiliated Family Practice training program. We offer a competitive remuneration package to include salary, malpractice insurance, time off, and flexible scheduling. Send CV to Empire Medical Group, PO Box 3571, San Bernardino, CA 92413.

PHYSICIANS WANTED

BEAUTIFUL COLORADO—Family Practice, Internal Medicine, and Occupational Physicians. Send CV to D. A. Franklin, MD, Medical Director, HealthWatch Medical Centers, 3400 Industrial Lane, Ste A, Broomfield, CO 80020.

INTERNIST BC/BE to assume busy established practice. Share call with three other Internists. Excellent hospital and family oriented community. University affiliation possible. Send CV to Search Committee, PO Box 1564, Redlands, CA 92373.

BROOKINGS, OREGON. Evening and weekend clinic. Family practice or emergency experience preferred. $35 per hour. Send CV to Art B. Wong, MD, FACEP, Emergency Physicians' Medical Group, 1 Maritime Plaza, Ste 710, San Francisco, CA 94111.

FAMILY PRACTICE PHYSICIAN. Southern California, Los Angeles suburb. BC/BE FP desired for group practice. Join five residency trained FPs in comprehensive practice. OB optional. Excellent hospital and support services. Salary, production, and benefits commensurate with experience. Malpractice paid. Send CV or call Mr Ed Myatt, Executive Director, Northridge Community Medical Group, 8330 Reseda Blvd., Northridge, CA 91324; (818) 886-1376.

GASTROENTEROLOGIST BC/BE to be a second Gastroenterologist in a 36 physician multispecialty clinic. Guaranteed salary and immediate full participation in incentive program. Excellent benefit package with excellent recreational, cultural, and educational opportunities. Send CV to Search Committee, Walla Walla Clinic, 55 West Tietan, Walla Walla, WA 99362.

OB/GYN. Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, Administrator, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

NEW MEXICO. BC/BE Primary Care Physician for 500-bed psychiatric/geriatric hospital. Exciting programs in an exciting location, with superb climate, recreational and cultural benefits. Base salary $70,017 plus optional on-call salary supplement to $10,000. Fringe benefits are 21%, including paid malpractice and license fees, 2.5% per year retirement. Contact Philip Taulbee, MD, Medical Director, Las Vegas Medical Center, Box 1388, Las Vegas, NM 87701; (505) 425-6711.

OREGON—FAMILY PRACTITIONERS, INTERNISTS, PEDIATRICIANS. Private practice opportunities are immediately available in beautiful northwest Oregon. Call today to investigate this opportunity to practice challenging medicine in a hospital-supported surrounding, while enjoying an incomparable lifestyle in one of the Northwest's most scenic areas. Competitive first year guarantees offered to the selected candidate. Interview and relocation expenses absorbed by the client. For complete details, contact Jim Murphy, Spectrum Search, PO Box 27352, St. Louis, MO 63141; 1 (800) 237-6906; (314) 878-2280.

NORTHERN CALIFORNIA, EMERGENCY MEDICINE. Full-time positions available in the Emergency Department at the University of California, Davis, Medical Center. The University serves a large region of northern California and is a major trauma center. Emergency physicians teach and supervise medical students and housestaff (240 per year) in addition to treating patients. Emergency Department physicians also provide medical control for UCDMC Life Flight, director of base station activities, and are actively involved in trauma care. Opportunities exist for involvement in other UCD School of Medicine teaching activities. Applicants should send CV to Robert W. Derlet, MD, Chief, Division of Emergency Medicine, University of California, Davis, Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817.

(Continued on Page 124)

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(Continued from Page 116)

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Opportunities are currently available for Board Certified or Board Eligible Family Practioners, Pediatricians, and Internists to serve our members in the San Francisco East Bay Area.

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GENERAL SURGEON—BE/BC. Outstanding opportunity for aggressive surgeon with a highly profitable, well-established, fee-for-service, multispecialty clinic. 14 physicians on staff. Ready made practice. Unmatchable guaranteed salary first year, then ownership. New hospital. Wonderful family town with nationally recognized school system and unequalled outdoor recreation possibilities. Telephone calls will not be accepted. Send CV to John Brust, Mesaba Clinic, 1814 14th Ave East, Hibbing, MN 55746.

CHAIRMAN, DEPARTMENT OF INTERNAL MEDICINE, KERN MEDICAL CENTER. A county operated teaching hospital is seeking a chairman for this UCLA affiliated department. The department has nine full-time and part-time members, 18 residency positions all currently filled with quality graduates. Qualifications: BC in Internal Medicine, established record of scholarly achievement in teaching and patient care, demonstrated management skills to direct a fully accredited residency program in an active public hospital and relate to other programs at Kern Medical Center and the UCLA system. Candidate must be eligible for appointment to senior faculty position at UCLA and be licensed in the State of California. (The County of Kern is an Equal Opportunity Employer.) Address inquiries with CV to Paul Toot, MD, Chairman, Internal Medicine Search Committee, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

NEW MEXICO—FAMILY PHYSICIAN. Innovative practice in New Mexico mountain community needs third BC/BE FP. Salary guarantee with reasonable work schedule. Video available showing our practice style, area, and people. Gila Family Care, 1121 West St, Silver City, NM 88061.

PHYSICIANS WANTED

INTERNIST, BC, to join four others in a busy practice in pleasant Sierra foothills community. Abundant recreational opportunities, yet near urban centers. Contact Dennis Nousaine, MD, FACP, 815 Court St, Ste 7, Jackson, CA 95642.

FAMILY PRACTITIONER. Visalia Medical Clinic has an opening for a BC/BE Family Practitioner to join a four physician department. Located in the San Joaquin Valley of California, serving a market area of approximately 350,000 citizens, the Visalia Medical Clinic is a 40 physician multispecialty clinic. Excellent hospital services and facilities. Compensation is incentive oriented with advancement to full partnership after one year. Excellent fringe benefits. John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

UTAH. Full-time physicians needed for urgent care centers in Ogden area. Send CV to Val Rollins, MD, Emergency Department, St. Benedicts Hospital, 5475 S. 500 East, Ogden, UT 84405; or call (801) 479-2376.

INTERNIST NEEDED FULL-TIME. Primary Care position for Board certified Internist is now available with a growing San Francisco Health Plan. The position includes both inpatient and outpatient responsibilities. Send CV to Medical Director, French Health Plan, 4131 Geary Blvd, San Francisco, CA 94118.

INTERNAL MEDICINE—CENTRAL UTAH. Seeking General Internist and/or Internist with subspecialty in Endocrinology or Infectious Disease to join established Internal Medicine clinic. 350-bed hospital across the street. First year salary with possible partnership after first year. Inquire: Dorothy Farnworth, Central Utah Medical Clinic, 1055 North 500 West, Provo, UT 84601.

THE IRVINE MEDICAL CENTER AND THE UNIVERSITY OF CALIFORNIA-IRVINE, DEPARTMENT OF RADIOLOGICAL SCIENCES are seeking a full-time faculty member for the Department of Radiological Sciences at the Clinical Associate Professor or Clinical Professor level who would be assigned as Director of the Department of Radiology at Irvine Medical Center. The Irvine Medical Center is a new 177-bed hospital currently under construction in Irvine, California. Hospital opening is scheduled for fall of 1988. Administrative experience and academic background, including teaching and/or research, is required. Please send CV and the names of five references to Richard M. Friedenberg, MD, Professor and Chairman, Department of Radiological Sciences, University of California, Irvine, 101 City Drive South, Orange, CA 92668. The University of California is an Affirmative Action and an Equal Opportunity Employer.

CALIFORNIA, SAN FRANCISCO BAY AREA. Full-time career Emergency Physician wanted for high volume Emergency department. Emergency Medicine BC/BE mandatory to participate in a group of twenty full-time staff physicians seeing over 300 patients per day. Salaried position, excellent benefits include three weeks paid vacation, one week CME, paid malpractice, health and life insurance, corporate shareholdership in three years. Send CV or contact David Gallagher, MD, 27400 Hesperian Blvd, Hayward, CA 94545.

TUOLUMNE. Sierra Foothills, Yosemite area—base station hospital with 12,000 visits per year. Openings for experienced Emergency Room MDs. Outstanding mountain, recreation area in the heart of California gold country. Fee-for-service approximately $40 per hour or greater. Please send CV to Art B. Wong, MD, FACEP, Emergency Physicians' Medical Group, 1 Maritime Plaza, Ste 710, San Francisco, CA 94111.

CARDIOLOGIST, BC/BE. Invasive Cardiologist with PTCA skills to join two FACC Cardiologists in expanding ten physician Internal Medicine group in San Diego. Position available July 1988 or sooner. Reply with CV, statement of interest, and three letters of reference, to F. C. Millward, Administrator, 5111 Garfield St, La Mesa, CA 92041.

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Enjoy professional challenge and growth with a successful and expanding HMO in southern California. CIGNA Healthplans of California is seeking Specialists and Primary Care physicians committed to concepts of prevention and health maintenance to join our facilities in Los Angeles and Orange Counties. We offer an excellent compensation and benefits package including profit sharing. For consideration, please forward CV to:

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INTERNIST. To join two Primary Care Internists in private practice in beautiful far-northern California one hour below major center. Midway between Portland and San Francisco, we have a rural setting with sophisticated practice and excellent hospital facilities. Subspecialty interest desirable within primary care framework. Salary and benefits with partnership an early goal. CV and your interests to R. H. Alley, Jr, MD, 105 Oberlin Rd, Yreka, CA 96097.

CALIFORNIA. BE/BC Internist to join staff of eight Internists in 15 physician multispecialty group located in central San Joaquin Valley. Competitive starting salary and full benefits. Excellent living and practice environment. Send CV to David A. Hellstern, Administrator, Kaweah Medical Group, Inc., 222 W. Willow, Visalia, CA 93291.

BC/BE CARDIOLOGIST. To join three invasive/noninvasive Cardiologists in practice, Portland, Oregon metropolitan area. Send CV to Number 76, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

ONCOLOGIST/INTERNIST. BC/BE to join 21 physician primary care and multispecialty group practice in beautiful Pacific Northwest setting. Reply to Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

CALIFORNIA. BC/BE Pediatrician to join staff of three Pediatricians in 15 physician multispecialty group located in central San Joaquin Valley. Competitive starting salary and full benefits. Excellent living and practice environment. Send CV to David A. Hellstern, Administrator, Kaweah Medical Group, Inc., 222 W. Willow St, Visalia, CA 93291.

ESTABLISHED BC FAMILY PRACTITIONER in south central Washington seeks BE/BC associate with OB interest. Practice in rural, family-oriented community serving area of 45,000. Income guarantee and assistance with relocation. Ski at White Pass. Fishing and other water sports on nearby Rimrock Lake and Columbia River. Contact PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-2070, ext 202.

BE/BC FAMILY PRACTICE physician wanted to join young successful BC Family Practitioner to start new group in northeastern Colorado community. Includes OB. Service area of 25,000. Generous first year income guarantee and assistance with relocation. Only one and one-half hours from Denver. Contact PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-2070, ext 202.

PACIFIC NORTHWEST, NEAR EUGENE, OREGON. BE/BC Internist wanted to join Family Practice group. Share call with Internists. Minimum salary guarantee. Good schools/outdoor recreation; University of Oregon/cultural events within 30 minutes. Contact John Hoopes, Cottage Grove Hospital, 1340 Birch St, Cottage Grove, OR 97424; (503) 942-0511.

CALIFORNIA—NORTH SAN FRANCISCO BAY AREA. Excellent opportunity for BC/BE Family Practitioner to join growing department. Flexible starting date. Multispecialty clinic emphasizing personalized care. Full hospital privileges including ICU/CCU. No obstetrics. Very favorable call schedule. Prepaid HMO practice provides excellent salary, benefits. Forward CV to Steven Freedman, MD, Kaiser Permanente, 1550 Gateway Blvd, Fairfield, CA 94533; (707) 427-4260.

PHYSICIANS WANTED

NEAR STANFORD. Six Internists, all subspecialty trained and members of clinical faculty at Stanford, interested in an Associate with subspecialty interest and training. Should be well grounded in Internal Medicine. Send CV to Dr Bigler, El Camino Internal Medical Group, 125 South Dr, Mountain View, CA 94040.

IDAHO. Family Practitioner with interest in OB wanted to join three Family Practitioners serving scenic northern Idaho community. Hospital provides complete assistance—office, salary, full benefits. BE/BC and cesarean section experience required. Enjoy outdoor recreation, rural life-style. Contact Jean Erickson, PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220-4199; (503) 256-2070.

SAN FRANCISCO BAY AREA multispecialty group seeks Internist, BC/BE, to join 26 congenial men and women delivering quality care in a combined fee-for-service, HMO/PPO setting. Bay Valley Medical Group, Attn: Don Lass, 27212 Calaroga Ave, Hayward, CA 94545; (415) 785-5000.

FAMILY PRACTICE. San Diego. Primary care FP/IM wanted for busy community health center. Spanish speaking preferred. Send résumé to LHFHC, 1809 National Ave, San Diego, CA 92113 or contact Bea Romo (619) 234-8171.

SOUTH CENTRAL WASHINGTON COMMUNITY seeks BE/BC Internist for solo practice. Share office space with two other physicians. First year income guarantee and other assistance. Great income potential for right candidate! Progressive 38-bed hospital has CT services. Excellent schools and recreation. Contact PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-4488.

CALIFORNIA CENTRAL VALLEY. Desire BC/BE Family Practitioner to join busy two man Family Practice. Easy drive to San Francisco or mountains. Growing area; city of 40,000; good schools. Guarantee plus benefits. Reply to Number 59, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PULMONARY INTERNIST. Practice opportunity in beautiful pacific northwest coastal town. BE/BC. Critical care skills needed. Must be affable and assertive. Send CV to Number 78, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

FAMILY PRACTITIONER—BC/BE. For Family Practice in a large central California community and migrant health center located in the San Joaquin Valley serving large Hispanic and Southeast Asian medically underserved population. Competitive salary with excellent fringe benefits and paid malpractice. Send CV and inquiries to Director, Sequoia Community Health Foundation, Inc., 2790 S. Elm Ave, Fresno, CA 93706.

EXCELLENT TEXAS OPPORTUNITIES in Cardiology, ENT, Family Practice (five), General Surgery, Internal Medicine (two), OB/GYN (four), Oncology, Orthopedic Surgery (three), Pediatrics (two), Vascular Surgery, Industrial Medicine. Excellent quality of life, first year guarantee, etc. Reply with CV or call Armando L. Frezza, Medical Support Services, 8806 Balcones Club Dr, Austin, TX 78750; (512) 331-4164.

NORTHERN CALIFORNIA OB/GYN. Beautiful Marin County, California OB/GYN practice looking for BC/BE female/male OB/GYN who is interested in joining a busy and successful practice of two MDs, one midwife, and four NPs. Progressive, busy OB practice offering family centered maternity care. Pro-choice philosophy. Opportunity for university affiliation. Lovely physical facilities with potential for investment. Must be well trained, enjoy working hard, committed to women's health care and fun to work with. Compensation package with partnership available in one year. Six weeks time off each year. Send résumé to WHMA/NEB, PO Box 1773, Ross, CA 94957.

PHYSICIANS WANTED

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John Short & Associates, Inc., an internationally recognized health care management and consulting firm, is actively seeking **PHYSICIANS** with experience and credentials in **FAMILY MEDICINE/GENERAL PRACTICE** and **PRIMARY CARE SPECIALTIES.**

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John Short & Associates Inc. offers competitive compensation including paid malpractice insurance, professional development fund and incentive programs. **For additional information please contact: Susan Bray, Recruiting Director, John Short & Associates, Inc., Box 1305, Columbia, MD 21044.**

BC/BE INTERNIST to associate with General Surgeon, OB/GYN, Pediatrician, Internist, and three FPs in well-established rural practice. Send CV to R. F. LeBlond, MD, Park Clinic, Box 1139, Livingston, MT 59047.

INTERNIST. Live in San Francisco and commute to nearby rural area for four two-night shifts per month in combined Internal Medicine/Emergency room practice. Four Internists currently working in stable group. Practice quality medicine in the country where you can make a greater impact and enjoy lots of free time wherever you like to live. 72k per year. Charles Rath, MD, 199 E. Webster St, Colusa, CA 95932; (916) 458-7739.

NORTHERN SAN FRANCISCO BAY AREA: Seeking Physician BC/BE in Internal Medicine for Internist position in growing department. Kaiser Permanente Medical Center, 1550 Gateway Blvd, Fairfield, CA 94533; (707) 427-4200.

WALK-IN PHYSICIAN WANTED. ER/Primary Care training preferred, outstanding opportunity to start new department in rapidly growing multispecialty fee-for-service clinic in east San Gabriel Valley. Excellent salary and incentives. Send CV or call Mr Ghormley, Administrator, 420 W. Rowland St, Covina, CA 91723; (818) 331-6411.

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UNIVERSITY OF CALIFORNIA, Irvine, Department of Medicine is seeking a full-time faculty person as General Internist for expanding academic group practice. Combined fee-for-service/capitation. Duties include 80-90% clinical practice in multispecialty faculty clinic, 10-20% teaching residents and students ambulatory care and inpatient medicine. Division of General Internal Medicine with strong commitment to teaching, practice, and research. Competitive salary and benefits. Affirmative action/equal opportunity employer. Send CV to Jeremiah Tilles, MD, UCI, Department of Medicine, Route 81, 101 City Drive South, Orange, CA 92668.

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WASHINGTON. Full-time Emergency Physician needed for moderate volume ED in Yakima area. $85,000 possible plus partial malpractice coverage. Near mountains, skiing, etc. Two and one-half hours from Seattle. Send CV to Ted Palmatier, MD, FACEP, 110 South Ninth Ave, Yakima, WA 98902, or call (509) 575-5060.

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Interested candidates should forward a CV, name, address and phone numbers of three references with other relevant material to:

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FAMILY PHYSICIANS, BC/BE, full- and part-time positions available with Obstetrics optional, to work with multispecialty group practice in the Seattle area. Attractive salary benefits. Contact Sharon Courlas, MD, (206) 326-4147. Send CV to Pacific Health Associates, 1200 12th Ave South, Seattle, WA 98144, Attn: Mary Anderson.

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DERMATOLOGIST. 55 physician multispecialty medical group seeks full-time BC/BE Dermatologist. Attractive compensation and benefits. Starting date negotiable. Send CV to Don Robertson, Administrator, The Moore-White Medical Group, 266 S. Harvard Blvd, Los Angeles, CA 90004.

BC/BE INTERNIST. In northern California wine country. Join two man group in private practice of Internal Medicine. Subspecialty interest OK. Reply to Number 81, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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Primary care physicians needed to work as *locum tenens* throughout California. High salary, paid malpractice. Work whenever you like. Permanent placements as well. Contact: Carol Sweig, Director, northern California, (415) 673-7676; Valerie Oblath, Director, southern California, (800) 437-7676.

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Rocephin® (ROCHE)® IV·IM
ceftriaxone sodium/Roche

Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms

LOWER RESPIRATORY TRACT INFECTIONS caused by *Strep. pneumoniae, Streptococcus* species (excluding enterococci), *Staph. aureus, H. influenzae, H. parainfluenzae, Klebsiella* species (including *K. pneumoniae*), *E. coli, E. aerogenes, Proteus mirabilis* and *Serratia marcescens*

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Staph. aureus, Staph. epidermidis, Streptococcus* species (excluding enterococci), *E. cloacae, Klebsiella* species (including *K. pneumoniae*), *Proteus mirabilis* and *Pseudomonas aeruginosa*

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by *E. coli, Proteus mirabilis, Proteus vulgaris, M. morganii* and *Klebsiella* species (including *K. pneumoniae*)

UNCOMPLICATED GONORRHEA (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae*, including both penicillinase and nonpenicillinase producing strains

PELVIC INFLAMMATORY DISEASE caused by *N. gonorrhoeae*

BACTERIAL SEPTICEMIA caused by *Staph. aureus, Strep. pneumoniae, E. coli, H. influenzae* and *K. pneumoniae*

BONE AND JOINT INFECTIONS caused by *Staph. aureus, Strep. pneumoniae, Streptococcus* species (excluding enterococci), *E. coli, P. mirabilis, K. pneumoniae* and *Enterobacter* species

INTRA-ABDOMINAL INFECTIONS caused by *E. coli* and *K. pneumoniae*

MENINGITIS caused by *H. influenzae, N. meningitidis* and *Strep. pneumoniae*. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by *Staph. epidermidis* and *E. coli*

SURGICAL PROPHYLAXIS. Preoperative administration of a single 1 gm dose may reduce incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated (*e.g.*, vaginal or abdominal hysterectomy) and in those for whom infection at the operative site presents serious risk (*e.g.*, during coronary artery bypass surgery)

Although ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery. When administered before indicated surgical procedures, a single 1 gm dose provides protection from most infections due to susceptible organisms for duration of procedure

SUSCEPTIBILITY TESTING. Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing

CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics), therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin *in vitro*.

Mild cases of colitis respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should also be considered.

Rarely, shadows suggesting sludge have been detected by sonograms of the gallbladder in asymptomatic and symptomatic patients. This appears to be reversible on discontinuation of therapy. In a few symptomatic patients receiving higher than usual doses who underwent surgery, sludge containing traces of ceftriaxone was recovered from surgical specimens. Discontinue therapy in patients who develop signs or symptoms suggestive of gallbladder disease; consider conservative management.

PRECAUTIONS: *GENERAL*. Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is excreted via both biliary and renal excretion (see Clinical Pharmacology). Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction, however, in patients with both hepatic dysfunction and significant renal disease, Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations.

Alterations in prothrombin times have occurred rarely in patients treated with Rocephin. Patients with impaired vitamin K synthesis or low vitamin K stores (*e.g.*, chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Rocephin treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Prolonged use of Rocephin may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Carcinogenesis. Considering the maximum duration of treatment and the class of the compound, carcinogenicity studies with ceftriaxone in animals have not been performed. The maximum

duration of animal toxicity studies was six months.

Mutagenesis. Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured *in vitro* with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Impairment of Fertility. Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.

PREGNANCY. Teratogenic Effects. Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects. In rats, in the Segment I (fertility and general reproduction) and Segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

NURSING MOTHERS. Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when Rocephin is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness of Rocephin in neonates, infants and children have been established for the dosages described in the Dosage and Administration section. *In vitro* studies have shown ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Exercise caution before administration to hyperbilirubinemic neonates, especially prematures.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed:

LOCAL REACTIONS – pain, induration or tenderness at the site of injection (1%). Less frequently reported (less than 1%) was phlebitis after I.V. administration.

HYPERSENSITIVITY – rash (1.7%). Less frequently reported (less than 1%) were pruritus, fever or chills.

HEMATOLOGIC – eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL – diarrhea (2.7%). Less frequently reported (less than 1%) were nausea or vomiting, and dysgeusia.

HEPATIC – elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin.

RENAL – elevations of the BUN (1.2%). Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM – headache or dizziness were reported occasionally (less than 1%).

GENITOURINARY – moniliasis or vaginitis were reported occasionally (less than 1%).

MISCELLANEOUS – diaphoresis and flushing were reported occasionally (less than 1%).

Other rarely observed adverse reactions (less than 0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the prothrombin time, jaundice, gallbladder sludge, glycosuria, hematuria, anaphylaxis, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations and epistaxis.

DOSAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily dose is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

For the treatment of serious miscellaneous infections in children, other than meningitis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams), given in divided doses every 12 hours.

Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days, in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered 1/2 to 2 hours before surgery is recommended.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least ten days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function; however, blood levels should be monitored in patients with severe renal impairment (*e.g.*, dialysis patients) and in patients with both renal and hepatic dysfunctions.

HOW SUPPLIED: Rocephin (ceftriaxone sodium, Roche) is supplied as a sterile crystalline powder in glass vials and piggyback bottles. The following packages are available:

Vials containing 250 mg, 500 mg, 1 gm or 2 gm equivalent of ceftriaxone, piggyback bottles containing 1 gm or 2 gm equivalent of ceftriaxone, bulk pharmacy containers containing 10 gm equivalent of ceftriaxone (NOT FOR DIRECT ADMINISTRATION).

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ADD-Vantage Vials** containing 1 gm or 2 gm equivalent of ceftriaxone.

Also supplied premixed as a frozen iso-osmotic, sterile, nonpyrogenic solution of ceftriaxone sodium in 50 mL single dose plastic containers† as follows:

1 gm equivalent of ceftriaxone, iso-osmotic with approximately 1.9 gm dextrose hydrous, USP added.

2 gm equivalent of ceftriaxone, iso-osmotic with approximately 1.2 gm dextrose hydrous, USP added.

NOTE: Rocephin in the frozen state should not be stored above -20°C.

*Registered trademark of Abbott Laboratories, Inc.

†Manufactured for Roche Laboratories, Division of Hoffmann-La Roche Inc., by Travenol Laboratories, Inc., Deerfield, Illinois 60015.

P.I. 0587

Roche Laboratories
(ROCHE) a division of Hoffmann-La Roche Inc.

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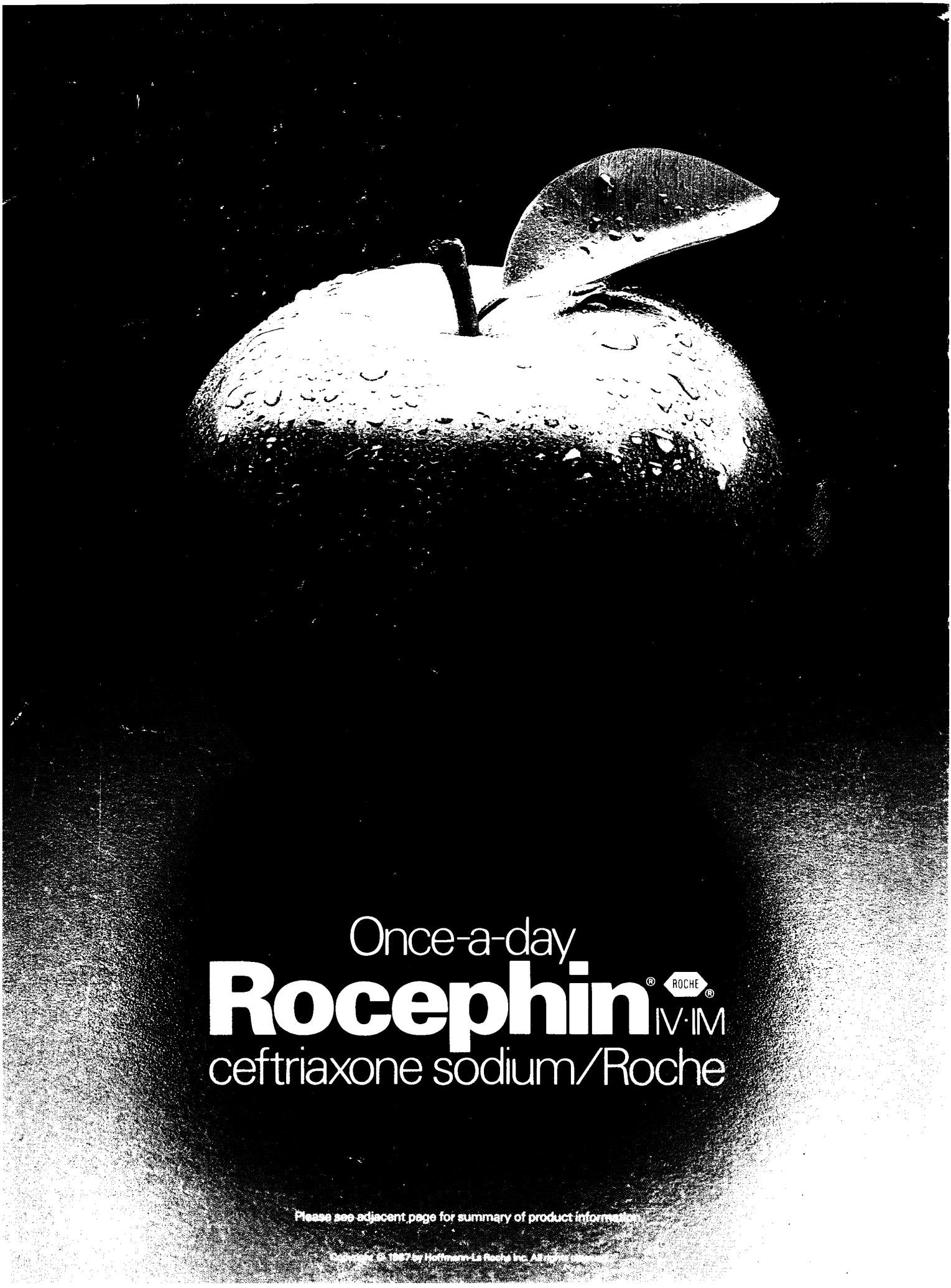
Once-a-day
Rocephin® ROCHE® IV·IM
ceftriaxone sodium/Roche
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